

REMARKS

The presently claimed invention concerns a method for biasing the amplification of the DNA molecules in a sample such that a nucleic acid molecule having a specific nucleotide at a selected position (e.g., a polymorphic site) is preferentially amplified relative to an otherwise identical nucleic acid molecule not having the specific nucleotide at the selected position. The method is useful for preferentially amplifying at least a portion of one allele of a gene relative to another, different allele of the gene in a sample containing both alleles of the gene as well as for other purposes.

Claims 10-16 are pending.

In an amendment filed on November 12, 2002, Applicants amended the claims to recite "two amplification primers that hybridize to both the first nucleic acid molecule and the second nucleic acid molecule at locations which flank the polymorphic site such that neither the first primer nor the second primer hybridizes to the polymorphic site" (language added by amendment underlined). The Applicants added this amendment in response to the Examiner's assertion in the Office Action mailed August 21, 2002 that "the limitation flank is broad and ...permits the inclusion of primer binding or hybridization regions to the polymorphic site." As explained in Applicant's remarks accompanying the November 12, 2002 amendment of the claims, "the commonly understood meaning of the term 'flank' excludes the possibility that the primers bind or hybridize to the polymorphic site."

In the Advisory Action mailed December 16, 2002, the Examiner stated that the "limitation 'such that neither the first primer nor the second primer hybridizes to the polymorphic site'...requires further consideration and search because the new limitation was not present in the previous claims." The Examiner went on to argue that "the original claims...were drawn to primers which flank the polymorphic site exemplified in page 8 of the specification. So, the focus on primers which do not hybridize to the polymorphic site will require further consideration and search."

Applicants disagree with the Examiner's position that the November 12, 2002 amendment added a new limitation. The phrase added in the November 12, 2002 amendment was not a new limitation. It is inherent in the term "flank." This much is clear from the commonly understood meaning of the term "flank." For example, Webster's Ninth New Collegiate Dictionary (Merriam-Webster Inc., Springfield, MA (1983) provides the following definition of "flank": "to be situated to the side of; esp: to be situated on both sides of." The Examiner has not provided any evidence that the term "flank" could or should be interpreted otherwise. Indeed, the Examiner's reference to page 8 of the specification as exemplifying the original claims is illustrative of Applicants' position. The relevant passage on page 8 of the specification reads as follows.

Methods described in the present invention first use amplification (preferably PCR amplification) using amplification oligonucleotides (primers) flanking a polymorphic site. The 3' end of one of the primers is close, highly preferably within 16 nucleotides, of a polymorphic site in template DNA. The second primer may lie at any distance from the first primer on the opposite side of the polymorphic site providing effective amplification.

It is clear from this description that primers which "flank" the polymorphic site do not hybridize to the polymorphic site. Thus, in this example, the 3' primer is described as being "close" to the polymorphic site within the other primer is "on the opposite side of the polymorphic site." It is clear that neither primer hybridizes to the polymorphic site.

In the Advisory Action dated May 8, 2003, the Examiner stated that it was the limitation that "neither the first primer nor the second primer hybridizes to the polymorphic site" and not the limitation "flank" that raises new issues requiring further search and consideration. The Examiner argued that the limitation requires further search because, according to the Examiner, "this limitation includes primers with modified nucleotide(s) or with base analogs, or protein analogs (which do not hybridize to a polymorphic site), requires further consideration and search."

Applicant : Jeffrey Olson et al.
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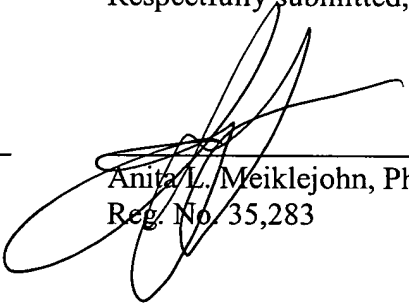
Applicants disagree with the Examiner's position. As explained above, the term "flank" excludes the possibility that either primer binds to the polymorphic site. Nevertheless, Applicants have filed this RCE and response so that the Examiner can consider the presently pending claims.

Nothing in the cited art, including Tygai et al. (U.S. Patent No. 6,277,607) teaches or suggests the presently claimed invention.

Enclosed is a Petition for Extension of Time with the appropriate fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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